Applicants: Ake R. Lindahl, *et al.*Serial No.: 09/700,177

Docket No.: <u>28069-558-NATL</u>

(Formerly: 003300-696)

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Listing of Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1.-56. (Canceled)

- 57. (Currently amended) A method of preparing a biologically active composition that includes a biologically active agent which can be released therefrom, the method comprising the steps of:
 - (a) supplying a composition including [a] one or more carrier starting substance substances having a property that the biologically active agent ean-be is either dispersed or dissolved therein up to a first degree of saturation;
 - (b) conducting chemical operations on the composition over a period of time, wherein the chemical operations chemically reacting the composition of step (a) over a period of time to form or cleave covalent bonds and result in the formation of a liquid or solid non-crystalline carrier matrix, the carrier matrix having a first property that the biologically active agent ean be is dispersed or dissolved therein up to a second degree of saturation, the second degree of saturation being greater than the first degree of saturation; and a second property that substantially inhibits precipitation of the biologically active agent is substantially inhibited after saturation of the biologically active agent in the composition; and
 - (c) adding the biologically active agent to the composition during the period of time for conducting the chemical operations of chemically reacting the composition, wherein said biologically active agent is present in an amount that saturates the one or more carrier starting substance substances and carrier matrix therein ccording to the first and second degrees of saturation, to form the biologically active composition.
- 58. (Previously presented) The method according to claim 57, wherein the biologically active agent is added above or around room temperature.

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59. (Canceled)

- 60. (Currently amended) The method according to claim [59] <u>57</u>, wherein the ehemical reactions comprise chemically reacting the composition comprises one or more reactions selected from etherifying, esterifying, etherification, esterification, hydrolysis, substitution, addition, elimination, oligomerization, or polymerization. oligomerising or polymerising reactions.
- 61. (Currently amended) The method according to claim 60, wherein the chemical reactions are selected and performed so as to provide chemically reacting the composition provides optimal delivery rate of the biologically active agent.
- 62. (Currently amended) The method according to claim 57, wherein the ehemical operations involve further comprising subjecting the carrier starting substance to a temperature of from around -50°C to around 300°C.
- 63. (Currently amended) The method according to claim 57, wherein the ehemical operations are conducted in step (b), the composition is chemically reacted for a time period of from 1 minute to 6 months.
- The method according to claim 57, wherein the one or more carrier starting substance substances, or mixture of two or more difference carrier starting substances, is selected from the group consisting of monomers, acids, alcohols, ketones, aldehydes, amines, amides, anhydrides, lactides, glycolides, saccharides, acrylic or acrylamide compounds, monomers of polyethylene oxide (PEO) PEO-diacrylate, cyanoacrylate, acrylate saccharides, acrylate lactate, acrylate glycolate, isocyanates, ethylene oxide, propylene oxide, pyrrolidone, PEO-diacrylate, ethylene-vinylacetate, monomers of organic siloxanes, and oligomers, polymers and prepolymers thereof.
- 65. (Currently amended) The method according to claim 64, wherein the acid is a monomeric acid and the alcohol is a monomeric alcohol, <u>and further</u> wherein the non-crystalline matrix comprises an ester or polyester thereof.

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monomeric acid is citric acid.

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66. (Previously presented) The method according to claim 65, wherein the

- 67. (Previously presented) The method according to claim 65, wherein the monomeric alcohol is propylene glycol.
- 68. (Previously presented) The method according to claim 57, wherein the biologically active agent is a pharmaceutically active agent.
- 69. (Currently amended) The method according to claim 68, wherein the pharmaceutically active agent is selected from the group consisting of guanosides, corticosteroids, psychopharmaceutical hormones, oxicams, peptides, proteins, antibiotics, antivirals, antimicrobials, anticancer agents, antifungals, estrogens, anti-inflammatory agents, neuroleptic agents, melanocyte stimulants, and gland stimulants and agents with an effect on affecting mast cell secretion.
- 70. (Currently amended) The method according to claim 57, wherein the second degree of saturation is increased with respect to the first degree of saturation due to chemical operations reaction such that the degree of dissociation, aggregation or degree of protonation of the biologically active agent in the carrier matrix is different from the degree of dissociation, aggregation or degree of protonation of the biologically active agent in the carrier starting substance.
- 71. (Currently amended) The method according to claim 57, wherein the biologically active agent is added at a predetermined point of time after the chemical operations have been initiated initiating the chemical reaction, the composition thus obtained then being further chemically reacted. subjected to the chemical operations.
- 72. (Previously presented) The method according to claim 57, wherein the biologically active composition consists of one liquid or solid phase only.
- 73. (Previously presented) The method according to claim 57, wherein the biologically active composition is used as a medicament.

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- 74. (Previously presented) The method according to claim 57, wherein the biologically active composition is applied topically to a mammal.
- 75. (Currently amended) The method [of] <u>according to</u> claim 64, wherein the acrylic or acrylamide type compounds are methacrylate.
- 76. (Currently amended) The method [of] <u>according to claim 71</u>, wherein said predetermined point of time is from 0.5 hours to 4 months after <u>initiating the chemical</u> reaction. the chemical operations have been initiated.
- 77. (Currently amended) The method [of] <u>according to claim 76</u>, wherein the composition is further <u>subjected to the chemical operations chemically reacted</u> for a time period from about 0.5 hours to 4 months.
- 78. (Currently amended) The method [of] <u>according to claim 69</u>, wherein the melanocyte stimulants and gland stimulants <u>are stimulators of stimulate</u> sebaceous and pilo-sebaceous glands.
- 79. (Currently amended) The method [of] <u>according to claim 74</u>, wherein the topical application is dermal.
- 80. (Currently amended) The method [of] according to claim 74, wherein the mammal is a human. man.
- 81. (Currently amended) The method [of] <u>according to claim 64</u>, wherein <u>the</u> acids are selected from the group consisting of mono-, di-, tri-acids and higher acids.
- 82. (Currently amended) The method [of] <u>according to claim 64</u>, wherein the alcohols are selected from the group consisting of mono-<u>alcohols</u>, [di-] <u>diols</u> and triols.
- 83. (Currently amended) The method [of] <u>according to claim 64</u>, wherein the acrylate saccharides are acrylate starch.

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84. (Currently amended) The method [of] according to claim 57, wherein said ehemical operations involve subjecting the composition to in step (b), the composition is chemically reacted at a temperature of from around 0°C to around 150°C.

85. (Canceled)

- 86. (Currently amended) The method [of] <u>according to claim 57</u>, wherein the <u>one or more carrier starting substances substance</u>, or the formed non-crystalline carrier matrix, acts as a solvent or dispersing medium.
- 87. (New) A process of preparing a biologically active composition, comprising:
 - (a) providing a carrier starting substance, or a mixture of two or more different carrier starting substances;
 - (b) dissolving or dispersing a biologically active agent to a first degree of saturation in the carrier starting substance, or the mixture of two or more different carrier starting substances; and
 - (c) subjecting the carrier starting substance, or mixture thereof, to a chemical reaction over a period of time to form or cleave covalent bonds so as to form a liquid or a solid non-crystalline carrier matrix in which the biologically active agent is present at a second degree of saturation that is higher than that of step (b), so as to form the biologically active composition;

wherein the chemical reaction of step (c) is initiated:

- (i) in the presence of the biologically active agent in an amount effective to obtain in the composition the second degree of saturation of the biologically active agent relative to the first degree of saturation of step (b); or
- (ii) in the absence of the biologically active agent, wherein the biologically active agent is added at a predetermined time after the chemical reaction is initiated, in an amount effective to obtain in the composition the second degree of saturation of the biologically active agent relative to the first degree of saturation

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of step (b), after which predetermined time the composition is further subjected to the chemical reaction.

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- 88. (New) The method according to claim 87, wherein the chemical reaction comprises one or more of etherification, esterification, hydrolysis, substitution, addition, elimination, oligomerization, or polymerization.
- 89. (New) The method according to claim 87, wherein the carrier starting substance, or a mixture of two or more different carrier starting substances is selected from the group consisting of monomers, acids, alcohols, ketones, aldehydes, amines, amides, anhydrides, lactides, glycolides, saccharides, acrylic or acrylamide compounds, monomers of polyethylene oxide (PEO)-diacrylate, cyanoacrylate, acrylate saccharides, acrylate lactate, acrylate glycolate, isocyanates, ethylene oxide, propylene oxide, pyrrolidone, PEO-diacrylate, ethylene-vinylacetate, monomers of organic siloxanes, and oligomers, polymers and prepolymers thereof.
- 90. (New) The method according to claim 89, wherein the acids are selected from the group consisting of mono-acids, di-acids, tri-acids and higher acids and the alcohols are selected from the group consisting of mono-alcohols, diols and triols.
- 91. (New) The method according to claim 89, wherein the acrylate saccharides are acrylate starch.
- 92. (New) The method according to claim 87, wherein the biologically active agent is a pharmaceutically active agent.
- 93. (New) The method according to claim 92, wherein the pharmaceutically active agent is selected from the group consisting of guanosides, corticosteroids, psychopharmaceutical hormones, oxicams, peptides, proteins, antibiotics, antivirals, antimicrobials, anticancer agents, antifungals, estrogens, anti-inflammatory agents, neuroleptic agents, melanocyte stimulants, gland stimulants and agents affecting mast cell secretion.

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94. The method according to claim 87, wherein the biologically active (New) composition consists of one liquid or solid phase only.

- 95. (New) The method according to claim 87, wherein the biologically active composition is used as a medicament.
- The method according to claim 87, wherein the biologically active 96. (New) composition is applied topically to a human or non-human mammal.
- 97. (New) The method according to claim 96, wherein the topical application is dermal.
- 98. The method according to claim 87, wherein, in step (c), the chemical (New) reaction is performed for a time period of from 1 minute to 6 months.
- 99. (New) The method according to claim 87, wherein, in step (c), the chemical reaction is performed for a time period from 0.5 hours to 4 months.
- The method according to claim 87, wherein the carrier starting 100. (New) substance, or mixture of two or more different carrier starting substances, is subjected to the chemical reaction at a temperature of from around -50°C to around 300°C.
- 101. The method according to claim 87, wherein the carrier starting (New) substance, or mixture of two or more different carrier starting substances, is subjected to the chemical reaction at a temperature of from around 0°C to 150°C.
- 102. (New) The method according to claim 87, wherein the second degree of saturation is increased with respect to the first degree of saturation due to the chemical reaction such that the degree of dissociation, aggregation or degree of protonation of the biologically active agent in the carrier matrix is different from the degree of dissociation, aggregation or degree of protonation of the biologically active agent in the carrier starting substance.

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103. (New) The method according to claim 87, wherein said predetermined point of time for adding the biologically active agent in step (c) is from 0.5 hours to 4 months after initiating the chemical reaction.

- 104. (New) The method according to claim 87, wherein, in (ii), said composition is further subjected to the chemical reaction from 0.5 hours to 4 months.
- 105. (New) The method according to claim 87, wherein the carrier starting substance, the mixture of two or more different carrier starting substances, or the formed non-crystalline carrier matrix, acts as a solvent or dispersing medium.
- 106. (New) The method according to claim 87, wherein the biologically active agent is dissolved or dispersed in the carrier starting substance, or mixture of two or more different carrier starting substances, at a temperature of about 25°C to 200°C.

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